Modulating Liver Sinusoidal Endothelial Cell Permeability to Enhance Engraftment of Endothelial Cell Progenitors for the Treatment of Hemophilia A

Grant Award Details

Modulating Liver Sinusoidal Endothelial Cell Permeability to Enhance Engraftment of Endothelial Cell Progenitors for the Treatment of Hemophilia A

Grant Type: Inception - Discovery Stage Research Projects

Grant Number: DISC1-08855

Project Objective: The objective of this project is to test a hypothesis that manipulating vascular permeability with factors such as VEGF can improve engraftment of liver sinusoidal epithelial cells (LSEC), a population that produces Factor VIII and is being investigated as a therapeutic approach for Hemophilia A.

Investigator:

Name:	Marcus Muench
Institution:	Vitalant Research Institute
Type:	PI

Disease Focus: Blood Disorders, Hemophilia A

Human Stem Cell Use: Adult Stem Cell, iPS Cell

Award Value: $180,000

Status: Closed

Progress Reports

Reporting Period: Year 2

View Report

Grant Application Details

Application Title: Modulating Liver Sinusoidal Endothelial Cell Permeability to Enhance Engraftment of Endothelial Cell Progenitors for the Treatment of Hemophilia A

Public Abstract:

Research Objective

We aim to demonstrate that regulators of endothelial cell permeability can foster engraftment of endothelial cell progenitors in the liver sinusoids leading to production of Factor VIII.

Impact

Our work would provide conceptual proof that a cell based therapy for hemophilia A is possible and should be pursued.

Major Proposed Activities

- Demonstrate that endogenous production of cytokine in mice with liver injury is responsible for the high engraftment of donor endothelial cells.
- Demonstrate that liver endothelial cells respond to regulators of endothelial cell permeability in the same manner as other types of endothelial cells.
- Demonstrate that administration of regulators of endothelial cell permeability can enhance the engraftment of human endothelial cells in the livers of immunodeficient mice.
- Demonstrate that endothelial progenitors generated from human induced pluripotent stem cells can engraft the livers of mice, produce Factor VIII and alleviate the symptoms of hemophilia A.

Statement of Benefit to California:

Hemophilia A is a life-threatening disease that affects about 1 in 5000 male births. Life-long therapy is required to help patients with this disease and this therapy suffers from complications from inhibitor production that can limit its benefits. Development of a cell therapy to treat hemophilia A may provide a long-lasting therapy or even cure for the disease greatly impacting the lives of the patients and the economic burden that the disease places on the patients and the medical system.
